Study the protective role of *Berberis vulgaris* aqueous extract on some Liver enzymes and proteins in male rats treated with Monosodium glutamate

***Abstract*---** Twenty adult male rats, ages 2-4 months, with an average weight of 150-300 g, have been utilized in the study. The rats have been split up to four groups (G), with five rabbits in each one of the groups. G1 was treated with normal saline extract 15ml orally as the positive control group, G2 has been treated with aqueous extract 14mg/kg as the negative control group, G3 has been treated with aqueous extract of Berberis vulgaris (300mg/kg BW), and G4 has been treated with aqueous extract of Berberis vulgaris (300mg/kg BW) following 3hrs. This study sought to ascertain protective effect of Berberis vulgaris extract on albumin, total protein, aspartate amino transaminase (ALT), globulin, alkaline phosphate (ALP), and alanine amino transaminase (AST). The current study's findings indicated that the mean levels of ALT, AST, ALP, albumin, total protein, and globulin have been much higher ($p \leq 0.050$) in G2 group than in G1 group. We have found no significant difference ($p \geq 0.050$) in levels of ALT, AST, total protein, ALP, albumin, and globulin in the group that had received doses of Berberis vulgaris (300mg/kg BW) and Monosodium glutamate (14mg/kg BW) in comparison with G1. We found a significant decrease ($p \leq 0.050$) in levels of (ALP, ALT, and AST) total protein, globulin, and albumin in G4 and G3 in comparison with G2.

***Keywords*:** Monosodium glutamate toxic, *Berberis vulgaris* extract, ALT, AST, ALP and proteins, rats.

Introduction

Therapeutic plants are presently the subject of intense academic interest. Saponins, phytic acids, phytates, proanthocyanidins, cardioprotective flavonoids, tannins, polysaccharides, lipids, and other phyto-components were found in various plant parts. Because of its widespread prevalence, barberry is considered a significant therapy for health difficulties associated with infectious infections. The fruit of the common herb barberry is utilized as food additive in many cultures as a medicinal plant. This shrub, which grows to a height of 1m to 3m, has barbed yellow wood and oval leaves with pendulous yellow flowers, which eventually turn into long, scarlet fruits that are 3 to 5 mm wide and 7 to 10 mm long. Those fruits are edible when they ripen in late summer and early fall. They include high levels of vitamin C and have a tart flavor (4,5). North America, Southern and central Europe, and Southern Asia are among the places in which this plant is found (6,7). This plant's many parts, like its stems, roots, leaves, and fruits, have been utilized in the traditional medicine in Iran as well as other countries (8). This plant has been utilized in the area of traditional medicine for several conditions, like the gastrointestinal problems, kidney stones, gallbladder and liver problems, circulatory system stimulation, and urinary tract disorders (9, 10). Berberis vulgaris is used for the treatment of several conditions because of its anti-bacterial, anti-hypertensive, anti-cancer, anti-oxidant, anti-inflammatory, and hepatoprotective properties (11). Triterpenoids, vitamin K, ascorbic acid, at least 10 phenolic compounds, and over 30 alkaloids are found in

Berberis vulgaris. In Berberis vulgaris, berberine is the main alkaloid that is extracted (12). According to research, it has anti-triglyceridemic, anti-oxidant, anti-bacterial, anti-cancer, anti-parasitic, anti-diabetic, and anti-hepatotoxic properties. Plant roots, stems, and leaves are used as powerful tonic and for therapeutic uses, which include sickness treatment, in the Middle East, Europe, and the US (13). In addition to that, Berberis vulgaris root extract is efficient at treating and preventing calculi development in the renal system (14). Monosodium glutamate (MSG), a non-essential amino acid in human body, has been widely used as amino additive since 1909 as a result of its characteristic umami flavor. Monosodium glutamate is frequently found in foods like tomatoes, cheese, fermented soy products, and yeast extracts. It is mostly absorbed in the small intestine when it enters the human body (15). The following binding of TAS1R1-TAS1R3 promotes intracellular calcium release, which in turn activates the umami flavor of monosodium glutamate, a taste area in the brain. Monosodium glutamate may have harmful effects on people, which include metabolic syndrome, cancer, immunological dysfunction, neurotoxicity, cardiovascular disease, fetal underdevelopment, infertility, and renal toxicity, according to mounting experimental and clinical data. Additionally, studies suggest that nutraceuticals and medicinal herbs couldy mitigate or reverse the negative effects of monosodium glutamate (16). The purpose of this research is to ascertain how the aqueous extract of Berberis vulgaris affects certain proteins and enzymes that are induced by Monosodium glutamate in male rats.

Methods and Materials

Materials

Preparation of aqueous extract of *Berberis vulgaris*

From the Baghdad Governorate in Iraq, a Berberis vulgaris plant was obtained. After being washed and chopped into little pieces, the plants have been processed into a fine powder with the use of an electric grinder. A total of 30g of dry Berberis vulgaris powder were taken via a sensitive scale, Sartorius type, and put inside a 1000ml glass flask, which contains 500ml of distilled water. The solution was after that covered and left at room temperature for 24hrs before being filtered by Whatman filter paper No. 101. The filtrate was after that taken and the sediment was left, and the filtrate was then put in clean, sterilized metal dishes and put inside an electric oven at 40 degrees for 24. Put the dry extract (17) in glass bottles and store them in refrigerator until the time that they are needed.

Experimental animals

Beginning on December 27, 2023, and ending on January 27, 2024, this study was carried out. There were twenty adult male Albino rats in this study, ages 2-4 months, with average weights of 150-300 g. The animals have been raised at a 25^{o}C temperature, with water and adequate ventilation under controlled conditions. Before the experiment began, the animals were given two weeks to acclimate. Twenty rats have been utilized in the present study; they have been split up to 4 groups, with five male rats in every group being treated differently.

1. Group I, the negative control group, received 15 milliliters of normal saline orally as a control.

2. Monosodium glutamate (MSG) at a level of (14mg/kg B.W.) has been administered orally to Group 2's Positive Control group for 30 days.

3. Berberis vulgaris extract was given orally to Group 3 rats for 30 days at a 300mg/kg B.W. dose.

4. Group 4 received MSG (14mg/kg B.W.) for 30 days after receiving (300mg/kg BW) of Berberis vulgaris extract orally.

Methods

Serum liver enzymes analysis

All groups' blood serum was centrifuged at 3000rpm for 15min. in order to extract the serum, which was after that stored in a refrigerator at a low degree of temperature (-20^{o}C) for the purpose of performing the required physiological tests, including measuring ALT and AST levels using method (18) and ALP using method (19).

Total protein, globulin and albumin estimation.

The blood serum's total protein content was determined with the use of technique (20), albumin levels were determined using method (21) and globulin levels were determined using approach (22).

Statistical Analysis: Every total calculated with a one-way ANOVA at the significance level was regarded as a significant value ($p < 0.05$) (23).

Results and Discussion

By analyzing the liver enzyme levels in the animals' serum during the course of our 30-day experiment, we discovered that MSG significantly raises ($p \leq 0.050$) levels of ALP, ALT, and AST in comparison to G1. We could not detect any significant difference ($p \geq 0.050$) between the group that had received doses of MSG (300mg/kg BW) and Berberis vulgaris (14mg/kg BW). Additionally, as shown in table (1), the Berberis vulgaris (300 mg/kg B.W) G3 significantly lowers ($p \leq 0.050$) levels of ALP, ALT, and AST compared with G1. After a month of oral MSG administration at a dose of 15mg/kg, the liver enzyme levels of male rats increased. This outcome aligned with the research of (24,25). When male rats were given MSG with drinking water at a 4g/L concentration per day for six weeks, Onobrudu and Barine (26) found that levels of liver enzymes increased. (27) showed that the same outcome was obtained when rats were given MSG daily for four weeks at a dosage of 2g/kg. Additionally, during six weeks, rats were given daily oral MSG at a dosage of 0.04–0.08 mg/kg in the study. The increased levels of liver enzymes ALP, AST, and ALT in the blood serum of rats given MSG were indicative of the substance's hepatotoxicity by all of the aforementioned researchers, despite the obvious variation in MSG concentrations and the varying administration durations. The substance's effect on producing damage, liver, and loss of hepatocytes might be the cause of the raised liver enzyme levels in the blood serum of the MSG group; as hepatocyte destruction increases, so does the secretion of these enzymes into the bloodstream (29). Additionally, this substance's generation of oxidative stress and creation of free

radicals will interact with unsaturated fatty acids in the liver cell membrane, causing the mitochondrial membranes to be destroyed and allowing such enzymes to leak (30,31).

Levels of aminotransferases ALT, AST and alkaline phosphatase ALP are an indicator of liver function through the presence or absence of liver cell dysfunction (32) and also result from the breakdown of L-glutamate (MSG) which turns into harmful glutamine inside liver cells, leading to their destruction and the release of their enzymes (33).

The elevation of MSG results in an increase in glutamate dehydrogenase (GDH) due to the release of amine groups as ammonia and the subsequent synthesis of ammonium ion ($NH4^+$), which is toxic and adversely impacts liver function. This effect results in liver damage and destruction, therefore causing the release of liver enzymes (34, 35).

We noticed from Table (1) that the aqueous extract of *Berberis vulgaris* works to reduce liver enzymes and prevents the damage resulting from the MSG. The results of the present study have been found consistent with the study of (24,36, 37,38).

The cause may be a result of the protective function of barberry on the liver cell membrane, resulting in decreased liver enzyme levels. Consequently, this plant functions to preserve the physiological activity of the liver. Chemical study of the plant revealed the presence of active compounds including berberine, berbamine, oxyacanthine and palmatine. These compounds are therapeutically significant and utilized in disease treatment due to their antioxidant, antibacterial, anticancer, and anti-inflammatory characteristics (36).

The aqueous extract also inhibits the production of reactive oxygen radicals due to its strong antioxidant activity. A study indicated that giving rats aqueous extract of barberry at a concentration of (25-50-100) for 11 months improved liver function by reducing enzyme activity. This indicates that the plant has many medicinal properties, which makes the plant have a protective role in protecting liver tissue (39). It works to prevent damage to liver, kidney, heart and brain tissue and their safety (40).

Table (1) Effects of aqueous extract of *Berberis vulgaris* (300mg/kg B.W) on the level of liver enzymes in serum of the male rats that have been treated with MSG for 30 days

	ALP I/U	**AST I/U**	**ALT I/U**
Control negative group	**40.38 ± 0.75 a**	**28.40 ± 0.85 a**	**20.62 ± 0.46 a**
Control positive group Monosodium glutamate (14mg/kg BW)	**79.18 ± 3.81 b**	**68.66 ± 1.73 b**	**37.66 ± 1.33 b**
***Berberis vulgaris* (300mg/kg BW) third group**	**31.60 ± 0.98 C**	**20.24 ± 0.69 c**	**17.10 ± 0.51 c**
***Berberis vulgaris* (300mg/kg B.W) And Monosodium glutamate (14mg/kg B.W.)**	**38.20 ± 1.32 A**	**27.40 ± 0.82 a**	**21.08 ± 0.34 a**
LSD	**5.18**	**2.62**	**1.86**

P value Significant ≤ 0.05

Results in Table2 reveal a significant increase ($p \leq 0.050$) in globulin, albumin, and total protein levels in male rats administered MSG at a concentration of 14mg/kg body weight daily for 30 days, in comparison to negative controls. However, no significant differences ($p \geq 0.050$) were observed in globulin, albumin, and total protein levels between groups G3 and G4 and group G1.

Additionally, Table (2) highlights the positive effect of the aqueous extract of Berberis vulgaris (300mg/kg body weight) on protein levels. These findings align with the studies of (47, 48, 49, 50). The experiment had also shown a significant increase ($p \leq 0.050$) in serum globulin, albumin, and total protein levels in male rats treated with MSG, consistent with studies (42, 43, 44).

The increase in protein levels is attributed to MSG's toxic effect on liver tissue, leading to its degradation, which results in protein breakdown and release into the bloodstream. This also elevates albumin and globulin levels (30). One study indicated that prolonged daily MSG intake causes liver necrosis and cell breakdown or kidney damage, impairing the proximal convoluted tubules' ability to reabsorb protein due to reduced Na+/K+-ATPase activity (43, 45). Another study reported that orally dosing rabbits with MSG at 0.25–0.5–1 g/kg body weight for 14, 28, or 56 days led to an increased total protein rate (46).

Elevated levels of the amino acids may result in stimulating the synthesis of the albumin in the liver, with some hormones like the thyroxine, growth hormone, and insulin promoting the increase in the production of albumin. The higher levels of total protein and globulin that have been observed in the present study result from the MSG's impact on the metabolic dysfunction, reduced liver efficiency in the storage of vitamins and minerals, in addition to increased generation of the free radicals because of the hepatic damage and inflammation (44).

The oral administration of Berberis vulgaris' alcoholic extract results in reducing these 3 levels of proteins, which suggests that the plant has protective roles in the health of the liver through supporting the metabolic processes as well as improving the levels of total protein, albumin, and globulin. This effect results from the plant's capability in decreasing the reactive oxygen species (ROS) that are caused by the oxidative stress, due to its constituents like the potassium, magnesium, flavonoids, vitamins, and unsaturated fatty acids. These components are helpful in safeguarding against diseases at the same time as enhancing liver and kidney functions.

These findings are consistent with studies (47, 48). A study by (49) also found that oral administration of Berberis vulgaris aqueous extract for 2–4 weeks, either alone or alongside the toxic substance aflatoxin, preserved protein levels and decreased liver enzymes, urea, creatinine, and blood sugar levels. This supports the plant's role in preventing liver damage. Our results align with these findings. Prior research has shown a significant reduction in total protein and albumin levels following administration of an aqueous extract of barberry leaves at concentration levels of 40–80–120mg/kg daily for 6 weeks in rats treated with the carbon tetra-chloride (50).

Table (2) Effects of aqueous extract of *Berberis vulgaris* (300mg/kg B.W) on levels of Globulin, Albumin and Total protein in serum of male rats with MSG for 30 days

	Globulin mg/dl	Albumin mg/dl	Total protein mg/dl
Control negative group	**2.52 ± 0.09 a**	**4.16 ± 0.82 a**	**5.52 ± 0.18 a**
Control positive group Monosodium glutamate (14 mg/kg BW)	**3.76 ± 0.20 b**	**7.30 ± 0.37 b**	**8.56 ± 0.40 b**
***Berberis vulgaris* (300mg/kg B.W) third group**	**2.22 ± 0.07 ac**	**3.70 ± 0.11 a**	**4.84 ± 0.19 c**
***Berberis vulgaris* (300mg/kg B.W) And Monosodium glutamate (14 mg/kg BW)**	**2.56 ± 0.14 a**	**3.88 ± 0.27 a**	**5.32 ± 0.16 a**
LSD	**0.380**	**0.70**	**0.63**

P value Significant ≤ 0.05

Berberis vulgaris has significant potential to enhance protective functions by increasing liver enzyme and protein levels. These effects are attributed to the direct action of the plant extract on the liver.

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